DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-645/S-003 NDA 19-645/ S-007
NDA 19-645/ S-005 NDA 19-645/S-008
NDA 19-645/ S-006 NDA 19-645/S-009

Syntex (U.S.A.) Inc.
Attention: Lynn DeVenezia-Tobias
Program Manager, Drug Regulatory Affairs
3401 Hillview Ave.
Palo Alto, CA 94304

11 OCT 2001

Dear Ms. DeVenezia-Tobias:

Please refer to your supplemental new drug applications dated October 22, 1993, received October 25, 1993, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Toradol (ketoralac tromethamine) IV/IM.

We acknowledge receipt of your submissions dated:

April 15, June 28, July 8 and 20, 1994 (SLR-004);
August 22, 1996 and May 26, 1998 (SLR-005);
August 19, 1994, January 19, February 8 and 24, 1995 (SLR-006);
December 16, 1994, January 5, 1995 and May 26, 1998 (SLR-007);
October 6, 1997 and May 26, 1998 (SLR-008); and
August 26, 1998 (SLR-009).

These supplemental new drug applications provide for:

S-003:
Provides for changes to the chemical name, **ADVERSE EVENTS** and **DOSAGE AND ADMINISTRATION** sections.

S-005:
Provides for revisions to the **CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE, WARNINGS, PRECAUTIONS, DOSAGE AND ADMINISTRATION,** and **CLINICAL STUDIES** sections of the label to be in accordance with 21 CFR 201.57(f)(9)(iv), Pediatric Use.

S-006:
Provides for changes on the carton and container.

S-007:
Provides for the addition of a **BOXED WARNING**, and revisions to the **CONTRAINDICATIONS** and **WARNINGS** sections of the label.

S-008:
Provides for changes in the labelling to bring the labelling into conformance with the Division's NSAID Class labelling issued in a guidance December 20, 1996.

S-009:
Provides for revisions to the **CLINICAL PHARMACOLOGY** and **PRECUATIONS** sections in accordance with 21 CFR 201.57(f)(10), *Geriatric Use*.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted August 26, 1998, immediate container and carton labels submitted May 26, 1998).

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 19-645/S-003, S-005, S-006, S-007, S-008, S-009." Approval of these submissions by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Carmen DeBellas, Chief Project Management Staff, at (301) 827-2125.

Sincerely,

Jonca Bull, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research